

HW

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re A	Application of:)
JUAN	IBANEZ)
Serial	No. 10/621,229) Art Unit: 1617
Filed:	July 15, 2003))) Examiner: Jennifer M. Kim
For:	Use of Flumazenil in the Production of a)
	Drug for the Treatment of Alcohol)
	Dependency)

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

The citation of information on the attached Form PTO/SB/08 is made pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98. A copy of each cited item is enclosed.

The citation of this information does not constitute an admission of priority or that any cited item is available as a reference, or a waiver of any right the applicant may have under applicable statutes, Rules of Practice in patent cases, or otherwise.

Respectfully submitted,

Stephen C. MacDonald, Ph.D.

Reg. No. L0063

KILPATRICK STOCKTON LLP 1100 Peachtree Street; Suite 2800 Atlanta, Georgia 30309-4530 55979-0100 (55979-314589)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on September 7, 2005.

Stephen C. MacDonald, Ph.D. - Limited Reg. No. L0063

ATLLIB02 191481.1

PTO/SB/08A (08-00)

Approved for use through 10/31/2002 OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for Form 1449/A/PTO

INFORMATION DISCLOS STATEMENT BY APP

(use as many sheets as necessary

Sheet of 10

Con	nplete if Known
Application Number	10/621,229
Filing Date	July 15, 2003
First Named Inventor	Juan Ibanez
Group Art Unit	1614
Examiner Name	Jennifer Kim
Attorney Docket Number	55979-314589 (55979-0100)

				U.S. PATENT DOCUMENT	S	
Examiner Initials	Cite No.1	U.S. Patent Number	Document Kind Code ² (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1.	6,455,276		Le Bourdelles et al.	09-24-2002	
	2.	6,740,677		Xue et al.	05-25-2004	
	<u> </u>					
	<u> </u>					
_						
-						
		İ				

		Foreign Patent Document		cument		Date of Publication of	Pages, Columns, Lines, Where	T
Examiner Initials	Cite No. ¹	Office ³	Number⁴	Kind Code ⁵ (if known)	Name of Patentee or Applicant of Cited Document	Cited Document MM-DD-YYYY	Relevant Passages or Relevant Figures Appear	1
								L
								\perp
								Τ
								Γ
								T
								T
		1 1 -						Ť
								Ť
								t
	L. <u>.</u>	.1						_
		1						
Examiner Signature						Date Considered		

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard S_T.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 6Applicant is to place a check mark here if English language translation is attached.

			Complete if Known		
Substitute f	or Form	1449/A/PTO '	Application Number	10/621,229	
	NEC	RMATION DISCLOSURE	Filing Date	July 15, 2003	
			First Named Inventor	Juan Ibanez	_
,	STA	TEMENT BY APPLICANT	Group Art Unit	1614	
		(use as many sheets as necessary	Examiner Name	Jennifer Kim	
Sheet	2	of 10	Attorney Docket Number	55979-314589 (55979-0100)	
	· · · · · · · · · · · · · · · · · · ·	OTHER INFORMATION - NON P			
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL item (book, magazine, journal, serial, symp publisher, city			T ²
	3.	Bell, E.C., et al., "Response to Flumaze	enil in the Late Luteal F	Phase and Follicular Phase	
		of the Menstrual Cycle in Healthy Control Females," Psychopharmacology, Vol. 172,			
		pp. 248-254 (2004)	inor i orinares, i syenop		
	4.	^	C1	. D. I. G. 6	
	4.	Berezhnoy, D., et al., "Conformational			
		GABA _A Receptors Detected With a No	vel Technique," <i>J. Neul</i>	rochemistry, Vol. 92, pp.	
		859-866 (2005)			
	5.	Betz, C., et al., "Could a Common Biod	chemical Mechanism U	nderlie Addictions?." J.	
	•	Clin. Pharm. Ther., Vol. 25, No. 1, pp.		•	
		Cim. 1 harm. Ther., vol. 25, 140. 1, pp.	11 20 (2000) (11031140)	(Olly)	
	6.	Biggio, G., et al., "Molecular Mechanis	sms of Tolerance to and	Withdrawal of GABA(A)	
		Receptor Modulators," Eur. Neuropsyc			
		Receptor Woddiators, Bur. Wear opsyc	<i>nopharmacor.</i> , voi. 15,	, 110. 0, pp. 411-425 (2005)	
-	7.	Boehm, S.L., et al., "γ-Aminobutyric A	cid A Receptor Subuni	t Mutant Mice : New	
		Perspectives on Alcohol Actions," Biod	-		
		(2004)	memieur i marmacorogy	, voi. oo, pp. 1301 1002	
•	8.				
	0.	Buckley, S.T., et al., "GABAA Recepto	r ß Subunit mRNA Exp	pression in the Human	
		Alcoholic Brain," Neurochemistry Inte	rnational, Vol. 45, pp.	1011-1020 (2004)	
	9.	Casasola, C., et al., "Hyperexcitability	Induced by GABA Wit	hdrawal Facilitates	
		Hippocampal Long-term Potentiation,"	Neuroscience, Vol. 12	6, pp. 163-171 (2004)	
				-, pp	
	10.	Clark, M., "Sensitivity of the Rat Hippo	ocampal GABA Recep	otor a4 Subunit to	
		Electroshock Seizures, Neuroscience L	etters, Vol. 250, pp. 17	-20 (1998)	
		,			
	11.	Criswell, H.E., et al., "Effect of Zolpid	em on Gamma-aminob	utyric Acid (GABA)-	
		Induced Inhibition Predicts the Interact			
		in Several Rat Brain Regions," J. Phar.			
		(1995) (Abstract Only)	macor. Exp. Therp., Vo	1. 275, 110. 1, pp. 520 550	
	12.			T-CC	┼
	'-	Davies, M., "The Role of GABAA Rece	-		
•		Central Nervous System, J. Psychiatry	Neurosci., Vol. 28, No.	. 4, pp. 263-274 (2003)	
	13.	Devaud L.L, et al., "Bidirectional Alter	rations of GARA(A) Re	ecentor Subunit Pentide	
		Levels in Rat Cortex During Chronic E		•	
•				iu wililulawai, J.	
		Neurochem., Vol. 69, No. 1, pp. 126-13	50 (1997)		

miner Da	Date
and the same of th	Considered

¹Unique citation designation)umber. ²Applicant is to place a check mark here if English language translation is attached.

Under the Paperwork Reduction Act of 1995, no persons are rec	U.S. Patent and Trade	PTO/SB/08B (08-00) pproved for use through 10/31/2002 OMB 0651-0031 emark Office: U.S. DEPARTMENT OF COMMERCE mation unless it contains a valid OMB control number
•	Cor	nplete if Known
Substitute for Form 1449/A/PTO .	Application Number	10/621,229
INFORMATION DISCLOSURE	Filing Date	July 15, 2003
INFORMATION DISCLOSURE	First Named Inventor	Juan Ibanez
STATEMENT BY APPLICANT	Group Art Unit	1614
(use as many sheets as necessary	Examiner Name	Jennifer Kim
Sheet 3 of 10	Attorney Docket Number	55979-314589 (55979-0100)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
	14.	Devaud L.L, et al., "Chronic Ethanol Consumption Differentially Alters the Express of Gamma-aminobutyric acid _A Chain Reaction Analysis," Mol. Pharmacol., Vol. 48, No. 5, pp. 861-868 (1995)	
	15.	Devaud L.L, et al., "Influence of Gender on Chronic Ethanol-Induced Alterations in GABA _A Receptors in Rats," Brain Res., Vol. 796, Nos. 1&2, pp. 222-230 (1998)	
	16.	Devaud L.L, et al., "Sensitization of Gamma-Aminobutyric acid _A Receptors to Neuroactive Steroids in Rats During Ethanol Withdrawal," J. Pharmacol. Exp. Ther., Vol. 278, No. 2, pp. 510-517 (1996)	
•	17.	DuBois, D.W., et al., "Binge Ethanol Exposure Delays Development of GABAergic Miniature Postsynaptic Currents in Septal Neurons," <i>Developmental Brain Research</i> , Vol. 152, pp. 199-212 (2004)	
-	18.	File, S.E., et al, "Effects of Nitrendipine, Chlordiazepoxide, Flumazeil and Baclofen on the Increased Anxiety Resulting from Alcohol Withdrawal," <i>Prog. Neuropsychopharmacol. Biol. Psychiatry</i> , Vol. 16, No. 1, pp. 87-93 (1992) (Abstract Only)	
	19.	File, S.E., et al., "Benzodiazepine Withdrawal: Behavioural Pharmacology and Neurochemical Changes." <i>Biochem. Soc. Symp.</i> , Vol. 59, pp. 97-106 (1993) (Abstract Only)	
	20.	File, S.E., et al., "Flumazenil but not Nitrendipine Reverses the Increased Anxiety During Ethanol Withdrawal in the Rat," <i>Psychopharmacology</i> , Vol. 98, No. 2, pp. 262-264 (1989)	
	21.	Finn, D.A., et al., "Differential Change in Neuroactive Steroid Sensitivity During Ethanol Withdrawal," J. Pharmacology and Experimental Therapeutics, Vol. 292, No. 1, pp. 394-405 (2000)	
	22.	Follesa, P., et al., "Modulation of GABA _A receptor Gene Expression by Allogpregnanolone and Ethanol, Euro. J. Pharmacology, Vol. 500, pp. 413-425 (2004)	
-	23.	Follesa, P., et al., "γ-Hydroxybutyric Acid and Diazepam Antagonize a Rapid Increase in GABA _A Receptors α4 Subunit mRNA Abundance Induced by Ethanol Withdrawal in Cerebellar Granule Cells, <i>Molecular Pharmacology</i> , Vol. 63, No. 4, pp. 896-907 (2003)	
	24.	Green, K.L, et al., "The Influence of Menstrual Cycle Phase on Sensitivity to Ethanol- Like Discriminative Stimulus Effects of GABA _A -Positive Modulators, <i>Pharmacology Biochemistry and Behavior</i> , Vol. 64, No. 2, pp. 379-383 (1999)	

Examiner Date Considered	
--------------------------	--

Substitute for Form 1449/A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary

Sheet 4 of 10

Cor	nplete if Known
Application Number	10/621,229
Filing Date	July 15, 2003
First Named Inventor	Juan Ibanez
Group Art Unit	1614
Examiner Name	Jennifer Kim
Attorney Docket Number	55979-314589 (55979-0100)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²				
	25.	Grobin, A.C., et al., "The role of GABA(A) Receptors in the Acute and Chronic Effects					
		of Ethanol," Psychopharmacology (Berl.), Vol. 139, Nos. 1-2, pp. 2-19 (1998) (Abstract					
		Only)					
	26.	Grobin, A.C., et al., "Chronic Ethanol Administration Alters Immunoreactivity for					
		GABA _A Receptor Subunits in Rat Cortex in a Region-Specific Manner," Alcholosim,					
		Vol. 24, No. 8, pp. 1137-1144 (2000)					
	27.	Hanchar, H.J., et al, "Alcohol Effects on γ-aminobutyric Acid Type A Receptors: Are					
		Extrasynaptic Receptors the Answer?," Life Sciences, Vol. 76, pp. 1-8 (2004)					
	28.	Hirani, K., et al., "Evaluation of GABAergic Neuroactive Steroid 3alpha-hydroxy-					
		5alpha-pregnane-20-one as a Neurobiological Substrate for the Anti-Anxiety Effect of					
		Ethanol in Rats," <i>Psychopharmacology</i> (Berl.), (Epub ahead of print) (2005) (Abstract Only)					
	29.	Holtman, Jr., J.R., et al., "Modification of Morphine Analgesia and Tolerance by					
•		Flumazenil in Male and Female Rats," Euro. J. Pharmacology, Vol. 470, pp. 149-156					
		(2003)					
	30.	Janak, P.H., et al., "The Reinforcing Effects of Ethanol are Altered by the Endogenous					
		Neurosteroid, Allpregnanolone," Alcohol Clin. Exp. Res., Vol. 22, No. 5, pp. 1106-1112					
		(1998) (Abstract Only)					
	31.	Janis, G.C., et al., "Effects of Chronic Ethanol Consumption and Withdrawal on the					
		Neuroactive Steroid 3alpha-hydroxy-5alpha-pregnan-20-one in Male and Female Rates,	ľ				
		Alcohol Clin. Exp. Res., Vol. 22, No. 9, pp. 2055-2061 (1998) (Abstract Only)					
	32.	June, H.L., et al., "Ethanol Self-Administration in Freely Feeding and Drinking Rats;					
		Effects of Ro15-4513 alone, and in Combination with Ro15-1788 (Flumazenil),"					
		Psychopharmacology (Berl.), Vol. 115, No. 3, pp 332-339 (1994) (Abstract Only)					
	33.	Kang, M., et al., "Persistent Reduction of GABA(A) Receptor-Mediated Inhibition in					
		Rat Hipposcampus After Chronic Intermittent Ethanol Treatment," Brain Res., Vol. 709,					
		No. 2, p. 221-228 (1996) (Abstract Only)					
•	34.	Kang, M., et al., "Alteration in the Sensitivity of GABA(A) Receptors to Allosteric					
		Modulatory Drugs in Rat Hippocampus After Chronic Intermittent Ethanol Treatment,"					
-		Alcohol Clin. Exp. Res., Vol. 22, No. 9, p. 2165-2173 (1998) (Abstract Only)					
	35.	Knapp. D.J., et al., "SB242084, Flumazenil, and CRA1000 Block Ethanol Withdrawal-	1				
		Induced Anxiety in Rats," Alcohol, Vol. 32, pp. 101-111 (2004)					
	36.	Ma, L., et al., "Transcriptional Regulation of the Mouse Gene Encoding the α-4 Subunit					
		of the GABA _A Receptor," J. Biological Chemistry, Vol. 279, No. 39 pp. 40451-40461					
		(2004)					
Examiner		Date	•				
Signature		Considered					

Complete if Known Substitute for Form 1449/A/PTO **Application Number** 10/621,229 Filing Date July 15, 2003 INFORMATION DISCLOSURE First Named Inventor Juan Ibanez STATEMENT BY APPLICANT Group Art Unit 1614 (use as many sheets as necessary **Examiner Name** Jennifer Kim of 10 Attorney Docket Number 55979-314589 (55979-0100) Sheet 5

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
	37.	Mahmoudi, M.K., et al., "Chronic Intermittent Ethanol Treatment In Rats Increases	
		GABA (A) Receptor Alpha4-subunit Expression: Possible Relevance to Alcohol	
		Dependence," J. Neurochem., Vol. 68, No. 6, pp. 2485-2492 (1997) (Abstract Only)	
	38.	Mann, K., "Pharmacotherapy of Alcohol Dependence," CNS Drugs, Vol. 18, No. 8, pp. 485-504 (2004)	
	39.	Matthews, D.B., et al., "Differential Regulation of GABA(A) Receptor Gene Expression	
		by Ethanol in the Rat Hippocampus Versus Cerebral Cortex," <i>J. Neurochem.</i> , Vol. 70, No. 3, pp. 1160-1166 (1998) (Abstract Only)	
	40.	Mitsuyama, H., et al., "GABA(A) Receptor Alpha1, Alpha4, and Beta3 Subunit mRNA and Protein Expression in the Frontal Cortex of Human Alcoholics," Alcohol Clin. Exp. Res., Vol. 22, No. 4, pp. 815-822 (1998) (Abstract Only)	
٠	41.	Moy, S.S., et al., "Enhanced Ultrasonic Vocalization and Fos Protein Expression Following Ethanol Withdrawal: Effects of Flumazenil," <i>Psychopharmacology</i> , Vol. 152, pp. 208-215 (2000)	
	42.	Moy, S.S., et al., "Flumazenil Blockade of Anxiety Following Ethanol Withdrawal in Rats," Psychopharmacology, Vol. 131, pp. 354-360 (1997)	
	43.	Potokar, J., et al., "Flumazenil in Alcohol Withdrawal: A Double-Blind	
		Placebocontrolled Study," Alcohol, Vol. 32, No. 5, pp. 605-611 (1997)	
	44.	Sanna, E., et al., "Changes in GABA _A Receptor Gene Expression Associated with Selective Alterations in Receptor Function and Pharmacology After Ethanol Withdrawal," J. of Neuroscience, Vol. 23, No. 37, pp. 11711-11724 (2003)	
	45.	Savic, I., et al., "Feasibility of Reversing Benzodiazepine Tolerance with Flumazenil," Lancet, Vol. 337, pp. 133-137 (1991)	
•	46.	Schmitt, U., et al., "Free-choice Ethanol Consumption Under the Influence of GABAergic Drugs in Rats," Alcohol Clin. Exp. Res., Vol. 26, No. 4, pp. 457-462 (2002) (Abstract Only)	
	47.	Stanley, K.M., et al., "Impact of an Alcohol Withdrawal Syndrome Practice Guideline on Surgical Patient Outcomes," <i>Pharmacotherapy</i> , Vol. 23, No. 7, pp. 843-854 (2003) (Abstract Only)	

Examiner	Date	
Signature	Considered	

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

Complete if Known Substitute for Form 1449/A/PTO **Application Number** 10/621,229 Filing Date July 15, 2003 INFORMATION DISCLOSURE **First Named Inventor** Juan Ibanez STATEMENT BY APPLICANT Group Art Unit 1614 (use as many sheets as necessary **Examiner Name** Jennifer Kim Attorney Docket Number 55979-314589 (55979-0100) Sheet 6 of | 10

	T	OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
	48.	Sundstrom-Poromaa, I., et al., "Hormonally Regulated $\alpha_4\beta_2\delta$ GABA _A Receptors are a	
		Target for Alcohol," Nature Neuroscience, Vol. 5, No. 8, pp. 721-722 (2002)	
	49.	Uzbay, I.T., et al., "Effects of Flumazenil on Ethanol Withdrawal Syndrome in Rats,"	
		Arzneimittelforschung," Vol. 45, No. 2, pp. 120-124 (1995) (Abstract Only)	
	50.	Vanover, K.E., et al., "Positive Allosteric Modulators of the GABA _A Receptor:	
		Differential Interaction of Benzodiazepines and Neuroactive Steroids With Ethanol,"	
		Psychopharmacology, Vol. 141, pp. 77-82 (1999)	
=	51.	Vanover, K.E., "Effects of Benzodiazepine Receptor Ligands and Ethanol in Rats	
		Trained to Discriminate Pregnanolone," Pharmacology, Biochemistry and Behavior, Vol.	
		67, pp. 483-487 (2000)	
	52.	Verheul, R., et al., "A Three-Pathway Psychobiological Model of Craving for Alcohol,"	
		Alcohol & Alcoholism, Vol. 34, No. 2, pp. 197-222 (1999)	
	53.	Weinbroum, A., et al., "Flumazenil Potentiation of Postoperative Morphine Analgesia,"	
		Clin. J. Pain, Vol. 16, No. 3, pp. 193-199 (2000) (Abstract Only)	
	54.	White, J., et al., "Antagonism of a Nicotine Plus Midzaolam Discriminative Cue in	
		Rats," Behav. Pharmacol., Vol. 5, No. 3, pp. 351-355 (1994) (Abstract Only)	
	55.	Van Miert, AS, "Appetite-Modulating Drugs in Dwarf Goats, With Special Emphasis on	
		Benzodiazepine-Induced Hyperphagia and its Antagonism by Flumazenil and RO 15-	
		3505", J. Vet Pharmacol Ther., Jun; 12(2):147-56 (1989)	
	56.	Zheng, T.M., et al., "Chronic Flumazenil Alters GABA(A) Receptor Subunit mRNA	
		Expression, Translation Product Assembly and Channel Function in Neuronal Cultures,"	
		J. Pharmacol. Exp. Ther., Vol. 277, No. 1, pp. 525-533 (1996) (Abstract Only)	

-		* · · · · · · · · · · · · · · · · · · ·		
- 1				
- 1				
- 1	Examiner		D-4-	
- 1			Date	
	Signature		Compident	
	Oigi iatai C		Considered	

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

PTO/SB/08B (08-00)

Approved for use through 10/31/2002 OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Complete if Known Substitute for Form 1449/A/PTO **Application Number** 10/621,229 Filing Date July 15, 2003 INFORMATION DISCLOSURE First Named Inventor Juan Ibanez STATEMENT BY APPLICANT Group Art Unit 1614 (use as many sheets as necessary **Examiner Name** Jennifer Kim Attorney Docket Number Sheet 7 of 10 55979-314589 (55979-0100)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
	57.	Baldwin, H.A., et al., "Flumazenil Prevents the Development of Chlordiazepoxide	
		Withdrawal in Rats Tested in the Social Interaction Test of Anxiety,"	
		Psychopharmacology, Vol. 97, No. 3, pp. 424-426 (1989) (Abstract Only)	
	58.	Brooks-Kayal-A.R., et al., "Human Neuronal γ-Aminobutyric Acid _A Receptors:	
		Coordinated Subunit mRNA Expression and Functional Correlates in Individual Dentate	
		Granule Cells," J. Neuroscience, Vol. 19, No. 19, pp. 8312-8318 (1999)	
	59.	Ferrar, G., et al., "Increased Expression of the Neuropeptide γ receptor γ1 Gene in the	
	ŀ	Medical Amygdala of Transgenic Mice Induced by Long-term Treatment with	
		Progesterone or Alloprenanolone," J. Neurochemistry, Vol. 79, pp. 417-425 (2001)	
	60.	Frostholm, A., et al., "Harmaline-induced Changes in Gamma Aminobutyric Acida	
		Receptor Subunit mRNA Expression in Murine Olivocerebellar Nuclei," Molecular	
		Brain Research, Vol. 85, pp. 200-208 (2000)	
•	61.	Gee, KW et al., "A Putative Receptor for Neurosteroids on the GABAA Receptor	
		Complex: the Pharmacological Properties and Therapeutic Potential of Epalons", Crit	
		Rev Neurobiol. 1995; 9(2-3):207-27 (Abstract Only)	
	62.	Gulinello, M., et al., "Progesterone Withdrawal Increases the α4 Subunit of the GABA _A	
		Receptor in Male Rats in Association With Anxiety and Altered Pharmacology – A	
		Comparison With Female Rats," Neuropharmacology, Vol. 43, pp. 701-714 (2000)	
	63.	Gulinello, M., et al., "Anxiogenic Effects of Neurosteriod Exposure: Sex Differences and	
	-	Altered GABA _A Receptor Pharmacology in Adult Rats," J. Pharmacology and	
		Experimental Therapeutics, Vol. 305, No. 2, pp. 541-548 (2003)	
	64.	Hawkinson, J.E., "Substituted 3β-Phenylethynyl Derivatives of 3α-Hydroxy-5α-pregnan-	
		20-one: Remarkably Potent Neuroactive Steroid Modulators of γ-Aminobutyric Acid _A	
		Receptors," J. Pharmacology and Experimental Therapeutics, Vol. 287, No. 1, p. 198-	
		207 (1998)	
	65.	Hogenkamp, D.J., et al., "Synthesis and in Vitro Activity of 3β-Substituted-3α-	
•		Hydroxypregnan-20-ones: Allosteric Modulators of the GABA _A Receptor," J. Med.	
		Chem., Vol. 40, pp. 61-72 (1996)	
	66.	Hsu, F. et al., "Progesterone Withdrawal Reduces Paired-Pulse Inhibition in Rate	
		Hippocuampus: Dependence on GABAA Receptor α4 Subunit Upregulation," J.	
		Neurophysiol., Vol. 89, pp. 186-198 (2003)	
	67.	Krogsgaard-Larsen, P., et al., "GABAA Agonists and Partial Agonists: THIP	
		(Gaboxadol) as a Non-Opioid Analgesic and a Novel Type of Hypnotic," Biochemical	
		Pharmacology, Vol. 68, pp. 1573-1580 (2004)	

1	1	
Examiner	Date	
Signature	Considered	
<u> </u>	 _ 	

	to tapatwork reaction risk of the personnel and	Complete if Known		
Substitute for Form 1449/	A/PTO •	Application Number	10/621,229	
INFOR	MATION DICCLOCUDE	Filing Date	July 15, 2003	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary	First Named Inventor	Juan Ibanez		
STATE	MENT BY APPLICANT	Group Art Unit	1614	
(1	use as many sheets as necessary	Examiner Name	Jennifer Kim	
Shoot 9	of 10	Attorney Docket Number	55979-314589 (55979-0100)	

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS				
Examiner Cite Initials No.						
	68.	Holt, R.A., et al., "Chronic Treatment with Diazepam or Abecarnil Differently Affects				
		the Expression of GABA _A Receptor Subunit mRNAs in the Rat Cortex,"				
		Neuropharmacology, Vol. 35, Nos. 9 & 10, pp. 1457-1463 (1996)				
	69.	Lan, N.C., et al., "Differential Responses of Expressed Recombinant Human Gamma-				
		aminobutyric acidA Receptors to Neurosteroids," J. Neurochem., Vol. 57, No. 5, pp.				
		1818-1821 (1991) (Abstract Only)				
	70.	Lee, C., et al., "Effects of Benzodiazepine Receptor Antagonist, Flumazenil, on				
		Antinociceptive and Behavioural Responses to the Elevated Plusmaze in Mice,"				
		Neuropharmacology, Vol. 30, No. 12A, pp. 1263-1267 (1991) (Abstract Only)				
	71.	Medina, J.H., et al., "Overview-Flavonoids: A New Family of Benzodiazepine Receptor				
		Ligands," Neurochemical Research, Vol. 22, No. 4, pp. 419-425 (1997)				
	72.	Smith, S.S., et al., "Neurosteroid Administration and Withdrawal Alter GABAA Receptor				
•		Kinetics in CA1 Hippocamppus of Female Rats," J. Physiol., Vol. 567, Pt. 2. pp. 421-				
	ļ	436 (2005) (Abstract Only)				
	73.	Sur, C., et al., "Preferential Coassembly of α4 and δ Subunits of the γ-Aminobutyric				
		AcidA Receptor in Rat Thalamus," American Society of Pharmacology and				
		Experimental Therapeutics, Vol. 56, pp. 110-115 (1998)				
11.2	74.	Whittemore, E.R., et al., "Pharmacology of the Human Gamma-Aminobutyric acidA				
		Receptor Alpha 4 Subunit Expressed in Xenopus Laevis Oocytes," Mol. Pharmacol.,				
		Vol. 50, No. 5, pp. 1364-1375 (1996) (Abstract Only)				
	75.	Wisden, W., et al., "Cloning, Pharmacological Characteristics and Expression Pattern of				
		the Rat GABA _A Receptor Alpha 4 Subunit," FEBS Lett., Vol. 289, No. 2, pp. 227-230				
		(1991) (Abstract Only)				

Examiner	Date	
Signature	Considered	

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

Onder the Capetron Household Factor to Participate Control of the Capetron Control of the Capetro Control of the Capetron Control of the Capetro Control of the Capetro Contro				Complete if Known		
Substitute f	or Form 1449/A/PTO		•	Application Number	10/621,229	
			L DISCLOSUBE	Filing Date	July 15, 2003	
_		_	I DISCLOSURE	First Named Inventor	Juan Ibanez	
,	STATEMEN	IT I	BY APPLICANT	Group Art Unit	1614	
(use as many sheets as necessary				Examiner Name	Jennifer Kim	
Sheet	9	of	10	Attorney Docket Number	55979-314589 (55979-0100)	

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
	76.	Adkins, C.E., et al., "α ₄ β ₃ δ GABA _A Receptors Characterized by Fluorescence	
		Resonance Energy Transfer-derived Measurements of Membrane Potential," J.	
		Biological Chemistry, Vol. 276, No. 42, pp. 38934-38939 (2001)	
	77.	Akk, G., et al., "Activation of GABA(A) Receptors Containing the alpha4 subunit by	
		GABA and Pentobarbital," J. Physiol., Vol. 556, Part 2, , pp. 1-39 (2004)	
	78.	Banerjee, P.K., et al., "Alterations in GABAA Receptor al and a4 Subunit mRNA Levels	
		in Thalamic Relay Nuclei Following Absence-like Seizures in Rats," Experimental	
		Neurology, Vol. 154, pp. 213-223 (1998)	
	79.	Biggio, G., et al., "GABA _A -receptor Plasticity During Long-Term Exposure to and	
		Withdrawal from Progesterone," Int. Rev. Neurobiol., Vol. 46, pp. 207-241 (2001)	
•	80.	Burt, D.R., "Alpha Subunit Position and GABA Receptor Function," Science's STKE,	
		No. 270, PE5, pp. 1-2 (2005)	
•	81.	I 1 T. A	-
	"	Lovick, T.A., et al., "Changes in GABA _A Receptor Subunit Expression in the Midbrain	
	82.	During the Oestrous Cycle in Wistar Rats," <i>Neuroscience</i> , Vol. 131, pp. 397-405 (2005) Lujan, R., et al., "Glutamate and GABA Receptor Signalling in the Developing Brain,"	
	02.		
	83.	Neuroscience, Vol. 130, pp. 567-580 (2005) Mody, I., "Distinguishing between GABA _A Receptors Responsible for Tonic and Phasic	-
		Conductances," Neurochemical Research, Vol. 26, Nos. 8-9, pp. 907-913 (2001)	
	84.	Porter, B.E., et al., "Heterogeneous GABA(A) Receptor Subunit Expression in Pediatric	
		Epilepsy Patients," Neurobiol. Dis., Vol. 18, No. 3, pp. 484-491 (2005) (Abstract Only)	
	85.	Quirk, G.J., et al., "Inhibition of the Amygdala: Key to Pathological States?," Ann. N.Y. Acad. Sci., Vol. 985, pp. 263-272 (2003)	
	86.	Rissman, R.A., et al., "Subregional Analysis of GABAA Receptor Subunit mRNAs in the	
		Hippocampus of Older Persons with and without Cognitive Impairment," J. of Chemical	
		Neuroanatomy, Vol. 28, pp. 17-25 (2004)	
-	87.	Saitoh, K., et al., "Nigral GABAergic Inhibition Upon Mesencephalic Dopaminergic	
		Cell Groups in Rats," Eur. J. Neurosci., Vol. 19, No. 9, pp. 2399-2409 (2004) (Abstract	
		Only)	
	88.	Sedvall, G., et al., "Recent Advances in Psychiatric Brain Imaging," Acta Radiol. Suppl.,	
		Vol. 374, pp. 113-115 (1990) (Abstract Only)	
		7, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,	<u> </u>

Examiner	·	Date	
Signature		Considered	

¹Unique citation designation number. ²Applicant is to place a check mark here if English language translation is attached.

Substitute for Form 1449/A/PTO

Sheet 10

INFORMATION DISCLOSURE **STATEMENT BY APPLICANT**

(use as many sheets as necessary of 10

Cor	nplete if Known
Application Number	10/621,229
Filing Date	July 15, 2003
First Named Inventor	Juan Ibanez
Group Art Unit	1614
Examiner Name	Jennifer Kim
Attorney Docket Number	55979-314589 (55979-0100)

		OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²
	89.	Smith, S.S., et al., "GABA _A Receptor α4 Subunit Suppression Prevents Withdrawal	
		Properties of an Endogenous Steroid," <i>Nature</i> , Vol. 392, pp. 926-930 (1998)	
	90.	Yang, W., "Cloning and Characterization of the Human GABA _A Receptor Alpha 4	
		Subunit: Identification of a Unique Diazepam-Insensitive Binding Site," Eur. J.	
		<i>Pharmacol.</i> , Vol. 291, No. 3, pp. 319-325 (1995) (Abstract Only)	
	91.	Zheng, T.M., et al., "Changes in γ-aminobutyrate Type A Receptor Subunit mRNAs,	
		Translation Product Expression, and Receptor Function During Neuronal Maturation in	
		vitro," Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 10952-10956 (1994)	
	92.	Smith, A.J., et al., "Effect of α Subunit on Allosteric Modulation of Ion Channel	
- ,		Function in Stably Expressed Human Recombinant γ-Aminobutyric AcidA Receptors	
		Determined Using ³⁶ Cl Ion Flux," <i>Molecular Pharmacology</i> , Vol. 59, No. 5, pp. 1108-	
•		1118 (2001)	

Examiner Signature	Date Considered	